VERSION OF AMENDED CLAIMS SHOWING THE CHANGES MADE

IN THE CLAIMS:

Cancel claims 3, 37 and 38 without prejudice to introducing the same subject matter at a later time;

Amend claims 1, 4, 33, 39, 42, 43 as follows:

1. (Twice amended) A method for expressing a heterologous gene in hepatocytes in culture comprising:

   - providing replication defective hepadnavirus particles at a titer level competent to infect hepatocytes, wherein the region of the [~~pre-S or~~] S-gene of the hepadnavirus genome has been replaced with the heterologous gene of up to 800 basepairs, such that the expression of the heterologous gene is regulated by the regulatory sequences of [~~the pre-S or~~] the S-gene;
   - infecting hepatocytes with the hepadnavirus such that the heterologous gene is delivered into the hepatocytes and expressed in the hepatocytes, and wherein the replication defective hepadnavirus particles are one of human hepatitis B virus or duck hepatitis B virus particles

4. (Twice amended) The method of claim 42, wherein the heterologous gene replaces [~~a region of~~] the S-gene under control of [~~the~~] an endogenous S-promoter.

33. (Thrice amended) A replication defective hepadnavirus particle of the group consisting of human hepatitis B virus and duck hepatitis B virus, wherein a region of a [~~pre-S and~~] S-gene of the hepadnavirus genome [~~have~~] has been deleted and replaced by a heterologous gene such that the sequences [~~for RC and RII~~] that are essential for reverse transcription are retained.

39. (Thrice amended) A method of producing replication defective hepadnavirus particles of human hepatitis B virus and duck hepatitis B virus at a titer suitable for infecting hepatocytes in culture comprising:

- co-transfecting hepatocyte cells of a hepatoma cell line with:

  (i) replication defective hepadnavirus constructs, wherein a region of one of [~~a pre-S or~~] an S-gene of the hepadnavirus DNA has been replaced with a gene encoding a heterologous gene [~~while retaining one of an RC or RII signal~~], such that [~~the~~] expression of the gene encoding a cytokine is regulated by regulatory sequences of the S-gene; and

(iii) a helper construct for transcomplementing lacking viral gene products;

- culturing the hepatocytes until infectious viral particles are produced; and
- recovering the infectious particles.

42. (Twice amended) A method for producing replication defective recombinant hepadnavirus particles capable of expressing a heterologous gene in hepatocytes in culture comprising:

- replacing an S-gene in a hepatitis B virus genome with the heterologous gene <u>of up to 800 base pairs</u> such that the expression of the heterologous gene is regulated by an S-promoter;
- producing a replication deficient hepadnavirus by means of a helper plasmid transcomplementing viral gene products such that the lacking viral gene products are present;
- Infecting hepatocytes with the recombinant hepadnavirus in culture, whereby the heterologous gene is delivered into the hepatocyte and expressed in the hepatocyte, wherein the replication defective recombinant hepadnavirus particles are human hepatitis B virus particles.

43. (Twice amended) A recombinant hepatitis B virus genome, wherein an S-gene in the genome is deleted and replaced by a heterologous gene of up to 800 base pairs and wherein the genome is selected from the group consisting of recombinant human hepatitis B virus or recombinant duck hepatitis B virus, and wherein the sequences [~~for RC and RII that are~~] essential for reverse transcription are retained.

REMARKS

Record is made of a brief interview between applicant's representative and the Examiner which took place on November 27, 2002. The Examiner is thanked for his help and assistance as well as for the courtesies extended to Counsel at that time. As a result of the telephone conference, applicant now submits this amendment.

Applicant's amendments to the claims overcome each and every objection or rejection to the claims set forth in the Examiner's Official Action of July 28, 2002 in which claims 1-8, 33-39 and 41-50 were rejected under 35 U.S.C. 112, first paragraph because the specification, while being enabling for a method of expressing a heterologous gene in hepatocytes in culture, does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The scope of the amended claims are now believed to be fully supported by the specification.

In particular, claims 1, 42, and 43 were amended to include the number of base pairs of the heterologous gene. The number of base pairs is supported in the specification on page 10, lines 15-16 and on page 14, lines 22-23.

Furthermore, claims 33 and 39 were amended by deleting reference to 'pre-S'. Also the expressions RC and RII which the Examiner inquired about were deleted from claims 33 and 39.

Applicant has cancelled claims 3, 37 and 38, thus making the objection to claim 38 moot.

In view of the above, each of the presently pending claims in this application is believed to be in condition for allowance. In particular, as outlined in the rejections under 35 USC § 112, first paragraph, the scope of the claims follow the scope of the disclosure as outlined by the Examiner in the Official Action. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue.

Should the Examiner consider necessary or desirable any formal changes anywhere in the specification, claims and/or drawing, then it is respectfully requested that such changes be made by Examiner's Amendment, if the Examiner feels this would facilitate passage of the case to issuance. If the Examiner feels that it might be helpful in advancing this case by calling the undersigned, applicant would greatly appreciate such a telephone interview.

The Commissioner is hereby authorized to charge fees, which may be required, or credit any overpayment to Deposit Account No. 50-1747.

Respectfully submitted,

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